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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/577,489	05/25/2000	Ray W. Wood	029318/0596	7761

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Elan Drug Delivery, Inc. c/o Foley & Lardner
3000 K Street, N.W.
Suite 500
Washington, DC 20007-5109

EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	PAPER NUMBER
1616	

MAIL DATE	DELIVERY MODE
10/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/577,489	WOOD ET AL.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2008*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-36,39,40,42,43,51-60 and 64-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-36, 39-40, 42-43, 51-60, and 64-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5)☐ Notice of Informal Patent Application

6)☐ Other: _____.

DETAILED ACTION

Claims 28-36, 39-40, 42-43, 51-60, and 64-72 are pending. Applicants previously cancelled claims 1-27, 37-38, 41, and 44-50. Applicants have newly cancelled claims 61-63. Applicants have amended claims 42-43. Claims 64-72 are new. Receipt and consideration of Applicants' amended claim set, declaration, and remarks/arguments submitted on October 7, 2008 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments. The finality of the office action mailed July 23, 2008 is withdrawn.

Moot Rejections/objections

All rejections and/or objections of claims 61-63 cited in the previous office action mailed on July 23, 2008 **are moot**, because said claims have been cancelled.

Terminal Disclaimer(s)

The terminal disclaimer filed on February 4, 2004 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 6,264,922 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Priority

The instant application is a divisional of Application No. 08/948,216 (***filed 10/9/1997***), which has issued as U.S. Patent No. 6,264,922 and is a CIP of application 08/394,103, filed 2/24/1995 **and abandoned *on 7/2/1997***. Applicants, via the immediate parent application

(08/948,216) of the instant application, are claiming the benefit of prior-filed nonprovisional application No. 08/394,103 under 35 U.S.C. 120, 121, or 365(c). Copendency between the parent application (08/948,216) and the prior application (08/394,103) is required. Since parent applications, 08/948,216 and 08/394,103 were not copending, when parent application 08/948,216 was filed, the benefit claim to the prior-filed nonprovisional application, 08/394,103 is improper. Applicant is required to delete the reference to the prior-filed application from the first sentence(s) of the specification, or the application data sheet, depending on where the reference was originally submitted, unless applicant can establish copendency between the applications, 08/948,216 and 08/394,103. Thus, the effective filing date of the instantly pending claims is October 9, 1997, the filing date of the parent divisional, application No. 08/948,216

Election/Restrictions

On 8/15/01 the original examiner required a species election of a specific respiratory illness. On 9/17/01 Applicants responded and elected asthma as the respiratory illness, with traverse. On July 30, 2002 a restriction requirement additionally requiring a second species election of a therapeutic agent was mailed. In the May 20, 2002 response Applicants elected a method of delivering an aerosol to the lungs of a mammal and corticosteroids as the therapeutic agent with traverse. On September 10, 2007, Applicants amended the claims from claiming a method of delivering an aerosol to the lungs of a mammal to claiming a method treating a respiratory illness in a mammal. Because Applicants received an advisory action on 8/21/07 that did not address the change in statutory subject matter and an office action on the merits on 12/27/07, the restriction requirement of record is interpreted to include a method of treating a

respiratory illness in a mammal. The species elections for asthma as the respiratory disease and corticosteroids as the elected therapeutic agent are maintained and remain in effect.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 32 recites the broad recitation a polymer, and the claim also recites various polymeric species, such as polyvinyl alcohol, polyvinylpyrrolidone, various cellulose compounds (cellulose is a polymer), polyethylene

glycols, polyether sulfonate, polyethoxylated fatty acid compounds (e.g. polyoxyethylene castor oil), etc. which are the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28-36, 39-40, 42-43, 51-60, and 64-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over BECOTIDE® in view of Lovrecich (U.S. Patent No. 5,008,114) and Spear et al. (U.S. Patent No. 5,525,623), as evidenced by Radhakrishnan (U.S. Patent No. 5,049,389) and "Glaxo History" (accessed October 24, 2008 at www.gsk.com/about/history-noflash.htm#).

Applicant Claims

Applicants claim a method treating a respiratory illness in a mammal comprising the steps of (a) providing an aerosol composition comprising aqueous droplets having a particle size of less than 10 microns in diameter, wherein the droplets comprise (i) water, (ii) crystalline particles of beclomethasone having a submicron particle size, (iii) at least one surface modifier adsorbed on the surface of the crystalline beclomethasone particles, and (b) administering the aerosol composition to the lungs of a mammal, wherein the respiratory disease is selected from the group consisting of ***asthma***, emphysema, respiratory distress syndrome, chronic bronchitis, and cystic fibrosis.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

BECOTIDE® is **an aqueous suspension of beclomethasone dipropionate** that is administered via inhalation to treat asthma and was first made commercially available by Glaxo in 1972 ("Glaxo History"). Radhakrishnan was provided in part to demonstrate that BECOTIDE® is an aqueous suspension of beclomethasone dipropionate that is conventionally administered by nebulization (i.e. it is atomized from a nebulizer) to treat bronchial asthma (col.

5, lines 43-51). Radhakrishnan measured the liquid droplet particle size of aerosolized BECOTIDE® expressed as mass median aerodynamic particle size (MMAD) in units of microns (Figure 4). Radhakrishnan also demonstrates that particles with a size of less than 1.1 microns read the alveoli upon inhalation (Figure 3). According to Radhakrishnan's measurements, **approximately 15% of the droplets have a particle size of about 400 nm or less and ~ 95% of the liquid droplets have a size of 10 microns or less** (Figure 4 and col. 16, line 53 through col. 17, line 17).

Lovrecich teaches the compositions comprising nanometer-sized crystalline medicaments distributed in the pores of a microporous support with an average pore diameter between 5 and 150 nm (i.e. **the nanocrystals necessarily have an average size between 5-150 nm**) (col. 1, lines 42-47 and claim 1). The crystalline active agent may have **crystalline dimensions between 3 and 100 nm** (Lovrecich claim 2). Lovrecich's preferred medicaments are **low water-solubility medicaments**, such as and including **corticosteroids** (col. 2, lines 3-10). Suitable support materials are silicas, silicates, zeolites, aluminas, activated carbons, and microporous polymer substances (col. 2, lines 21-25). The nanocrystalline medicaments exhibit **improved biopharmaceutical properties, chemical and physical stability** and more prolonged and controlled release of the medicament (col. 2, line 51 through col. 3, line 11). Lovrecich's compositions may comprise additional excipients such as **gelatin (a surface modifier),** sorbitol, lactose, **starch (a surface modifier), magnesium stearate (a surface modifier), and sodium lauryl sulphate (a surface modifier).** Sodium lauryl sulfate is also known as sodium dodecyl sulfate. Starch reads on a polymer and polymers are necessarily surface modifiers, as evidenced by Applicants' claim 32.

Spear teaches that **jet nebulizers and ultrasonic nebulizers are conventional means of creating aerosols for use as asthma medication** (col. 13, lines 34-40).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

As far as can be ascertained at this time BECOTIDE® is silent as to the particle size and crystalline nature of the suspended beclomethasone dipropionate particles, as well as whether a surface active agent is adsorbed onto the surface of the crystalline beclomethasone particles and the quantity of surface modifier present. These deficiencies are cured by the teachings of Lovrecich.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to combine the teachings of BECOTIDE® and Lovrecich, because incorporation of Lovrecich's composition comprising nanometer-sized crystalline beclomethasone dipropionate (BDP), a corticosteroid, distributed in the pores of a microporous support into BECOTIDE® would afford compositions having improved chemical and physical stability of the active agent, as well as improved biopharmaceutical properties. An ordinary skilled artisan would have also been motivated to modify BECOTIDE® to utilize nanometer-sized crystalline beclomethasone particles to ensure that these particles efficiently reached the alveoli upon inhalation, because sub-micron particle sizes are art recognized as being suitable for ensuring adminstration to the alveoli upon inhalation administration. Regarding the limitation of a surface modifier being adsorbed onto the crystalline BDP, it is the Examiner's

position that Lovrecich's compositions comprising excipients such as sodium lauryl sulfate, starch, magnesium stearate, etc. (i.e. compositions containing a mixture of these components) would necessarily result in the adsorption of surface modifier upon the surface of the crystalline BDP. Regarding the administration of BDP to treat asthma, BDP is a conventionally utilized to treat asthma, thus an ordinary skilled artisan would have been motivated to utilize BDP to treat a disease for which it is indicated.

Regarding the particle sizes recited in Applicants' new claims. It is the Examiner's position that nanocrystalline BDP with a size between 5-150 nanometers would necessarily meet these limitations. The physical characteristics (e.g. size) of particulate compositions are clearly result specific parameters that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal physical particle characteristics (e.g. MMAD) of a particulate composition needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention.

Regarding the use of a jet nebulizer or an ultrasonic nebulizer to deliver the aqueous formulation, it would have been prima facie obvious to utilize a conventional nebulizer to administer formulations taught as being suitable for administration from a nebulizer, such as BECOTIDE®. An ordinary skilled artisan would have had a reasonable expectation of modifying BECOTIDE® per the teachings of Lovrecich, because provides the necessary guidance to obtain nanocrystalline BDP particles distributed in a solid support. The ordinary

skilled artisan would have a reasonable expectation of success, because there is nothing of record to suggest that the Lovrecich's compositions could not be subsequently suspended in the aqueous carrier of BECOTIDE®.

Regarding the amount of surface modifier present in the composition administered, the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention. Applicants' tabulated specification data is noted, and is not considered to demonstrate unexpected or surprising results. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Conclusion

Claims 28-36, 39-40, 42-43, 51-60, and 64-72 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571)

272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J.H.A.-A.
Patent Examiner
Technology Center 1600

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616